

Attorney's L ~~cket~~ No. 1032553-000037
Application No. 10/670,504

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AMENDMENTS TO THE CLAIMS:

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This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

Claims 1-42 (Canceled)

Claim 43 (New): A composition suitable for immediate application after mixing in situ, comprising a drug substance with low water solubility in molecular association in a liposome dispersion, wherein the composition is obtained by:

- a) providing in a first container said drug substance with low water solubility;
- b) providing in a second container a liposome dispersion in an aqueous medium, said liposome dispersion being optically clear;
- c) mixing in situ, the contents of said first container with the contents of said second container, yielding a composition being optically clear and enabling visual inspection for presence of precipitates or an unassociated drug substance, and providing a solubilized composition ready for immediate application.

Claim 44 (New): The composition according to claim 43, wherein said drug substance in said first container is provided as an amorphous powder which has been obtained by precipitation and/or lyophilization or milling, optionally with a stabilizer.

Claim 45 (New): The composition according to claim 43, wherein said drug substance in said first container is provided as a solution in a hydrophilic solvent.

Claim 46 (New): The composition according to claim 43, wherein the composition yielded after mixing the contents of said first and second containers comprises less than 15% w/w of a hydrophilic solvent.

Claim 47 (New): The composition according to claim 45, wherein said hydrophilic solvent in said first container is selected from the group consisting of ethanol, 96% ethanol, absolute glycerol, propylene glycol, ethyl lactate, polyethylene glycol 300, polyethylene glycol 400, 1,3 butandiol, succinic acid diethyl ester, triethyl citrate, dibutyl sebacate, dimethyl acetamide, DMSO, glycerineformal, glycofurool (tetraglycol), isopropanol, lactic acid butyl ester, N-methylpyrrolidone, solketol, propylene carbonate, propylene glycol diacetate, tetrahydrofurfuryl alcohol, diethylene glycol mono ethyl ether, triacetin and a combination thereof.

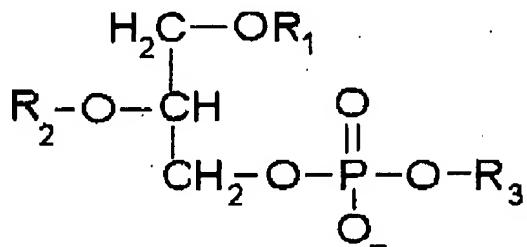
Claim 48 (New): The composition according to claim 43, wherein said optically clear liposome dispersion in said second container prior to mixing has a lipid concentration in the range between 0.5% w/w and 25% w/w and allows at least 40% of light to be transmitted at a wavelength of 660 nm using a 1 cm transmission cell or cuvette.

Claim 49 (New): The composition according to claim 48, wherein said composition yielded from mixing of the contents of said first and second containers has an optical clarity which is not decreased by more than 25% at a wavelength of 660 nm using a 1 cm transmission cell or cuvette as compared to the optical clarity of said liposome dispersion prior to mixing.

Claim 50 (New): The composition according to claim 48, wherein said optically clear liposome dispersion in said second container prior to mixing comprises from 5% w/w to 15% w/w of at least one membrane lipid.

Claim 51 (New): The composition according to claim 43, wherein said liposomal dispersion in said second container comprises phospholipids selected from the group consisting of phosphatidylcholine, phosphatidylethanolamine, sphingomyelin, phosphatidic acid, phosphatidyl inositol, phosphatidylserine and phosphatidylglycerol, glycolipids, gangliosides, cerebrosides and a combination thereof.

Claim 52 (New): The composition according to claim 51, wherein the phospholipid is of the formula



wherein R_1 represents $\text{C}_{10}\text{-C}_{20}$ acyl; R_2 represents hydrogen or $\text{C}_{10}\text{-C}_{20}$ acyl; R_3 represents hydrogen, 2-trimethylarnino-1-ethyl, 2-amino-1-ethyl, $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_1\text{-C}_5$ alkyl substituted by carboxy, $\text{C}_2\text{-C}_5$ alkyl substituted by carboxy and hydroxy, $\text{C}_2\text{-C}_5$ alkyl substituted by carboxy and amino, an inositol group or a glyceryl group or a salt thereof.

Claim 53 (New): The composition according to claim 43, wherein said liposome dispersion in said second container prior to mixing comprises lipid particles having an average particle size which is smaller than 300 nm.

Claim 54 (New): The composition according to claim 43, wherein said liposome dispersion in said second container prior to mixing comprises lipid particles having an average particle size which is smaller than 100 nm.

Claim 55 (New): The composition according to claim 43, wherein the ratio of said drug substance in said first container to the lipid in said liposome dispersion in said second container is between 1:2 to 1:200 parts by weight.

Claim 56 (New): The composition according to claim 43, wherein the contents of said first and said second containers, respectively, include stabilizers comprising isotonic and buffer agents, or preservatives comprising anti-microbials.

Claim 57 (New): The composition according to claim 44, wherein said first container contains said drug substance in the form of a lyophilized cake, including pharmaceutically acceptable excipients selected from the group consisting of polyethylene glycol 3000, polyethylene glycol 4000, a sugar and a combination thereof.

Claim 58 (New): The composition according to claim 43, wherein said first container comprises at least one excipient selected from the group consisting of membrane lipids, charged lipids, bile salts or salts of fatty acids, polysorbate 80, poloxamer and polyethoxylated castor oil, and a combination thereof.

Claim 59 (New): The composition according to claim 43, wherein each of the first and second containers is independently selected from the group consisting of ampoule, vial

with rubber stopper and cap, single and double chamber syringe, infusion bag or bottle, suitable for parenteral administration.

Claim 60 (New): A method for the preparation of a composition suitable for immediate application after mixing comprising a drug substance with low water solubility in molecular association in a liposome dispersion, said method comprising:

- a) providing in a first container said drug substance with low water solubility;
- b) providing in a second container a liposome dispersion in an aqueous medium, said liposome dispersion being optically clear;
- c) mixing in situ, just prior to application, the contents of said first container with the contents of said second container, yielding a composition which is optically clear and free from precipitates or an unassociated drug substance, and providing a solubilized composition ready for immediate application.

Claim 61 (New): The method of claim 60, wherein the method is used in one of medical applications, clinical research and pre-clinical screening applications, including in-vitro cell or in vivo animal efficacy/toxicity studies and for solubilizing compounds in lipid carriers that may be processed further for internal and external application.

Claim 62 (New): The method of claim 61, wherein said optically clear composition obtained by mixing the contents of said first and second containers is inspected visually for precipitates or an unassociated drug substance.

Claim 63 (New): The method of claim 60, wherein said optically clear composition yielded from the in situ mixing of said contents of said first and second containers is sterile for administration parenterally immediately after preparation.

Claim 64 (New): A method of administering the composition of claim 43, comprising administering the optically clear composition by injection.

Claim 65 (New): The method according to claim 64, wherein the step of administering the composition is conducted immediately after in situ mixing.

Claim 66 (New): The composition according to claim 43, wherein the composition is sterile.

Claim 67 (New): A method of administering the composition of claim 65, comprising parenterally administrating the composition.

Claim 68 (New): The method according to claim 67, wherein the step of administering the composition is conducted immediately after in situ mixing.

Claim 69 (New): The composition according to claim 57, wherein the sugar comprises mannitol, lactose, saccharose or a combination thereof.